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Abstract of the Disclosure

The present invention relates to DNA binding proteins comprising zinc finger domains in which two histidine and two cysteine residues coordinate a central zinc ion. More particularly, the invention relates to the identification of a context-independent recognition code to design zinc finger domains. This code permits identification of an amino acid for positions -1, 2, 3 and 6 of the  $\alpha$ -helical region of the zinc finger domain from four-base pair nucleotide target sequences. The invention includes zinc finger proteins (ZFPs) designed using this recognition code, nucleic acids encoding these ZFPs and methods of using such ZFPs to modulate gene expression, alter genome structure, inhibit viral replication and detect alterations (e.g., nucleotide substitutions, deletions or insertions) in the binding sites for such proteins. In addition, the invention provides a rapid method of assembling a ZFP with three or more zinc finger domains using three sets of 256 oligonucleotides, where each set is designed to target the 256 different 4-base pair targets and allow production of all possible 3-finger ZFPs (i.e.,  $>>10^6$ ) from a total of 768 oligonucleotides.

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